Evaluation of Plaque Protrusion Following Carotid Artery Stenting Using 3D-rotational Angiography

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Objective: Plaque protrusion is one of the current problems with carotid artery stenting (CAS) for carotid artery stenosis, and it may induce delayed postprocedural cerebral infarction. In this study, we evaluate the possibility of using three-dimensional rotational angiography (3DRA) to examine the stent lumen during CAS.

Methods: First, as a basic experiment, we determined the optimal contrast medium concentration for 3DRA. We then studied the presence or absence of plaque protrusion in 43 patients who underwent CAS at our hospital using 3DRA, intravascular ultrasound (IVUS), or DSA.

Results: Optimal contrast medium concentration was determined to be 50% by the basic experiment. In clinical evaluation, plaque protrusion was detected in 12 patients (27.9%) by 3DRA, compared to 7 (16.2%) by IVUS and in 3 (6.9%) by DSA. In patients where plaque protrusion was undetected by 3DRA, it was also undetected by IVUS and DSA after CAS.

Conclusion: Three dimensional rotational angiography appears to be useful for in-stent plaque protrusion detection.

Keywords ▶ carotid stenting, plaque protrusion, three dimensional rotational angiography

Introduction

In Japan, carotid artery stenting (CAS) began to be included in insurance coverage in 2007 as a treatment for carotid artery stenosis. Since then, it has been widely utilized and various stents and distal embolic protection devices have been introduced. Marked improvements in the therapeutic outcome have been reported. Cerebral infarction, a major complication of CAS, has been considerably reduced due to improvements in both the devices and preprocedural plaque diagnosis. Unresolved problems remain, however, including plaque protrusion. Plaque protrusion is regarded as a factor in inducing delayed cerebral infarction, which means intraprocedural and postprocedural evaluation of the stent lumen is important.1 Presently, examination of the stent lumen during CAS is performed primarily using intravascular ultrasound (IVUS),2 but the system requires lesion cross, involving a considerable risk of peripheral embolism. In this study, we evaluated the possibility of an alternative, low-invasive examination of the stent lumen by the use of three-dimensional rotational angiography (3DRA) as an alternative to IVUS examination.

Subjects and Methods

This study consisted of a basic experiment and clinical research.

Basic experiment

The experimental materials and methods were adopted from the report by Hosokawa et al.3) We prepared an experimental phantom by embedding a stented simulated vessel model in a plastic cervical phantom (110 mm in diameter, 180 mm long). A 2.5 mL syringe (Terumo Corporation,
Tokyo, Japan) was used as the simulated vessel. The stents used were the Precise stent (Cordis, Johnson & Johnson, Fremont, CA, USA), PROTAGE stent (Medtronic, Irvine, CA, USA), and Carotid Wallstent (Boston Scientific, Natick, MA, USA). The simulated vessel was filled with the Oypalomin 300 (300 mg Iodine/mL; Fuji Pharma Co., Ltd, Toyama, Japan) as a contrast medium at a concentration of 70, 50, 30, 20, 15, or 10%. The phantom was geometrically positioned at the isocenter between the X-ray tube and flat panel detector (FPD) (Fig. 1). We used the Allura Clarity FD20/15 (Philips Electronics Japan, Tokyo, Japan) angiography system.

Angiographic data of the simulated vessel phantom were processed using XtraVision, the angiographic system workstation (Philips Electronics Japan). Angiography was performed at a field of view (FOV) of 8 inches, the images were displayed in a 384×384 matrix. The optimal contrast medium concentration was determined by three radiology technicians and four neurosurgeons.

Clinical cases
Between July 2015 and November 2016, 43 of the 47 patients who underwent CAS at our hospital were evaluated, excluding three with a poor contrast effect and one with artifact due to pulsation of the carotid artery, where images were unreadable. Usual DSA and IVUS were performed at the end of CAS, and 3DRA was carried out after protection device removal. IVUS (Volcano, San Diego, CA, USA) was performed using an auto-pullback system (0.5 mm/sec). The conditions of 3DRA were as follows: the contrast injection rate was 5 mL/s, total injection volume was 30 mL, injection time was 6 seconds, and the FOV was 8 inches. Reconstruction was made in the exam preset mode using a 384×384 matrix, and we evaluated images displayed by multi-planar reconstruction (MPR). We defined plaque protrusion as a filling defect judged to be present in MPR images from three directions by 3DRA. DSA, IVUS, and 3DRA images were evaluated for the presence or absence of plaque protrusion by four neurosurgeons with clinical experience of 10 years or longer and three radiology technicians with clinical experience of 5 years or longer.

Results
Basic experiment
Figure 2 shows the results of imaging of the simulated vessels in which the Precise stent, PROTAGE stent, or Carotid Wallstent were embedded, the concentration of the contrast medium at which the stent and the lumen could be visually distinguished with minimum halation selected as optimal by the neurosurgeons and radiology technicians. As a result of image interpretation, we selected 50% as the contrast medium concentration for all stents.
Evaluation of Plaque Protrusion after CAS by 3DRA

Procedural diffusion-weighted magnetic resonance imaging showed hyperintensities in 8 of the 12 patients in whom plaque protrusion was detected by 3DRA, but in only 4 of the 31 patients in whom plaque protrusion was denied by 3DRA, with a significant difference in frequency (chi-square test, P < 0.05).

Clinical cases
The 43 patients consisted of 39 males and 4 females with a mean age of 73.3 years. Carotid artery stenosis was symptomatic in 25, including 2 who underwent emergency CAS for progressive stroke; it was asymptomatic in 18 patients. Protective devices were used for patients. In 24 patients, Precise stent was used, Carotid Wallstent in 14 patients, and PROTAGE stent in 4 patients. In one patient, the Precise stent and Carotid Wallstent were used concomitantly for a long lesion. No patients developed symptomatic intraprocedural cerebral infarction.

Of the 43 patients, plaque protrusion was detected in 12 (27.9%) by 3DRA, 7 (16.2%) by IVUS, and 3 (6.9%) by DSA.

In all cases where plaque protrusion was undetected by IVUS or DSA, it was also undetected by 3DRA.

Table 1 shows whether plaque protrusion was detected by each modality in the 12 patients in whom 3DRA detected plaque protrusion. In three patients who showed relatively large plaque protrusion, an additional stent-in-stent procedure was performed. In these three patients, plaque protrusion was detected at the end of the initial treatment by all three modalities. One patient developed visual impairment associated with central retinal artery occlusion 3 hours after returning to the ward. In the remaining nine patients in whom plaque protrusion was detected by 3DRA, no peripheral embolism was observed thereafter with additional postprocedural anticoagulant therapy. Post-procedural diffusion-weighted magnetic resonance imaging showed hyperintensities in 8 of the 12 patients in whom plaque protrusion was detected by 3DRA, but in only 4 of the 31 patients in whom plaque protrusion was denied by 3DRA, with a significant difference in frequency (chi-square test, P < 0.05).

Table 1  Detection of plaque protrusion with three different radiological diagnostic modalities. (+) detected (−) not detected

<table>
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DWI: diffusion weighted image; IVUS: intravascular ultrasound; 3DRA: 3D-rotational angiography

Case Presentations

Case 1
A 70-year-old man with a history of lumbar spinal canal stenosis was referred to our department after asymptomatic
left-internal carotid artery stenosis was detected by MRA following detailed examination after dizziness. Since about 80% stenosis was demonstrated by angiography (Fig. 3A), we decided to perform CAS.

By the right femoral artery approach, an 8 Fr Optimo stent (Tokai Medical, Aichi, Japan) was placed in the left common carotid artery. Thereafter, a PercuSurge stent (Medtronic) was inserted to the peripheral side of the site of stenosis, pre-dilatation (Rx Genity 4.0 mm × 30 mm, Kaneka Medics, Osaka, Japan) was performed with distal protection, and a PROTAGE tapered (10.7 mm × 40 mm) was placed. Since treatment was insufficient to cover the stenosed area of the common carotid artery, a Precise Pro Rx stent (10 mm × 30 mm) was placed additionally on the proximal side. The procedure was ended after postdilatation (aviator plus 5.5 mm × 30 mm; Cordis) (Fig. 3B). While a filling defect was noted on postprocedural 3DRA (Fig. 3C and 3D), plaque protrusion could not be confirmed by IVUS (Fig. 3E). Since the filling defect observed by 3DRA was also small, the patient was post-procedurally administered 60 mg of argatroban for 3 days in addition to dual-antiplatelet therapy and was discharged without ischemic symptoms.

**Case 2**

An 81-year-old male with a history of coronary artery stenting for acute myocardial infarction (2006) and surgery for abdominal aortic aneurysm (2009) developed transient left hemiplegia. Right internal carotid artery stenosis was detected by MRA, so he was referred to our hospital. At initial examination, no neurologic abnormalities were noted, except vascular murmur in the right cervical region. Angiography showed 70% stenosis at the bifurcation of the right carotid artery (Fig. 4A), so CAS was planned.

We selected an approach via the right brachial artery because of previous surgery for abdominal aneurysm, and a 6 Fr Sheathless (Asahi Intecc, Aichi, Japan) was placed.
Discussion

Carotid artery stenting for cervical internal carotid artery stenosis appeared in the mid-1990s as a non-invasive alternative for carotid endarterectomy (CEA), and it is long established as an effective therapy. As non-inferiority of CAS was demonstrated by the Stenting and Angioplasty with Protection in Patient at High Risk for Endarterectomy (SAPPHIRE) in a large-scale clinical study where CEA-high-risk patients were divided into CAS and CEA groups, it began to be covered by insurance in Japan in 2008. Subsequently, the Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST) also showed that both the safety and efficacy of CAS were comparable to those of CEA. Concerning periprocedural complications, however, both SAPPHIRE and CREST showed that there were more incidences of cerebral infarction associated
with CAS than CEA. Although the difference was not significant, the prevention of periprocedural cerebral infarction was recognized as a problem with CAS and needs to be resolved.

Intraprocedural cerebral infarction has decreased steadily with improvements in instruments such as the stent and embolic protection device and since the development of plaque diagnosis by preprocedural plaque imaging. On the other hand, delayed cerebral infarction, occurring within a few days after the procedure, is still observed with a fixed probability, remaining one of the current problems with CAS to be addressed. Although plaque protrusion is suggested to be a primary cause of delayed cerebral infarction, there remains no established preventive measure and at present, early detection is considered important. Shinozaki et al. compared plaque protrusion rates of detection between angiography and IVUS immediately after CAS in 77 consecutive patients, reporting that the detection rate was 2.6% by angiography alone, but 7.8% by IVUS, suggesting usefulness of IVUS. They treated patients in whom plaque protrusions were detected by additional percutaneous transluminal angioplasty (PTA) or stenting all without cerebral infarction. If plaque protrusion occurs, they concluded, it is manageable as long as it can be detected. Presently, a large amount of literature supports the usefulness of IVUS for detecting plaque protrusion. Although IVUS is safe, there seems to be a considerable risk of peripheral vascular embolism associated with the passage of devices through the stent lumen. In this study, we used 3DRA, which can be performed by a regular angiography system with improvements in devices. It can be used at many facilities and is considered less invasive and more versatile than IVUS, requiring no new additional procedures. Additionally, for 3DRA, the contrast medium is not injected at any higher volume than in regular angiography, so the technique is considered unlikely to increase peripheral vascular embolism due to plaque.

Okahara et al. reported that they started evaluation of plaque protrusion 1 week after CAS by CTA, but 3DRA is more advantageous in that the condition in the stent can be assessed immediately after the procedure, and additional procedures can be evaluated as necessary.

At present, we have no criteria regarding additional treatments, but we perform PTA at least in patients showing protrusion in the stent lumen on 3DRA if it remains unchanged or tends to increase with time. Furthermore, if PTA is ineffective we consider the addition of stents.

Hashimura et al. performed CTA, IVUS, and DSA after CAS in 32 patients to evaluate plaque protrusion reporting that plaque protrusion was noted in eight (25%) of the 32 patients as a result of examination of the presence or absence of plaque, particularly, by postprocedural CTA and IVUS.

Okahara et al. performed 3D-CTA after CAS and reported that CT low density was noted in 6 (26%) of their 23 patients. In all these reports, the detection rate was higher by contrast studies than by IVUS, so the detection rate by 3DRA in our present study (27.9%) is considered reasonable. This high detection rate by contrast studies compared with IVUS may be due to differences in plaque properties among the subjects in various studies. It is also considered possible, however, that not only plaque protrusions, but also thrombi, which IVUS is generally not good at detecting, are detected as filling defects by contrast studies. Stent thrombosis is also an important causative factor for delayed cerebral infarction, and is considered advantageous in that both thrombi and plaque protrusions can be detected. As the possibility of simple artifacts cannot be excluded, however, further validation with accumulation of cases is considered necessary.

Since none of the cases judged to be positive by IVUS or DSA were false negatives by 3DRA, it agrees with the consideration of being sufficiently reliable. There were also cases, however, in which images were unreadable due to artifact of body movements because of intrinsic limitations of 3DRA. There may also be artifacts derived from uneven contrast enhancement due to the blood flow in each patient, possibly leading to false-positive judgments. Improvements are required in imaging conditions including the position of the guiding catheter, through which the contrast medium is injected. While it is still necessary to continue evaluation with modifications in the above points in mind, the reliability of 3DRA for plaque detection protrusion is considered equal to, or higher than, that of IVUS.

Conclusion

3DRA shows potential usefulness in the detection of plaque protrusion in the stent after CAS.

Disclosure Statement

The authors have no conflicts of interest to disclose regarding this paper.
References